Dear friends of clinical journal club - load the file down at <u>https://www.mdc-berlin.de/cjc</u>. This website also gives you access to my seminar on Wednesdays 16:00 English and 17:00 German. You need to click on *Besprechung beizutreten*. If it fails to work immediately, keep on clicking.

A 44-year-old man with Crohn's disease that was being treated with infliximab presented with a 2-day history of a facial rash. In the previous week, his daughter had had a sore throat, and his mother had developed a similar rash on her face. His heart rate was 96 beats per minute, and his temperature was 36.6°C (97.9°F). Physical examination was notable for well-demarcated, warm, erythematous, confluent plaques on the cheeks, nose, and glabella. The pharynx was normal, and no cervical lymphadenopathy was observed. Which of the following is the most likely culprit organism for the underlying diagnosis? Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus pyogenes. The appearance is a classic. Years back, inhibiting aldosterone with spironolactone (introduced in 1959) was found to improve outcomes in heart failure patients. Steroidal mineralocorticoid receptor antagonists reduce morbidity and mortality among patients with heart failure and reduced ejection fraction, but their efficacy in those with heart failure and mildly reduced or preserved ejection fraction has not been established. Data regarding the efficacy and safety of the nonsteroidal mineralocorticoid receptor antagonist, finerenone, in patients with heart failure and mildly reduced or preserved ejection fraction are needed. The Finerenone Trial to Investigate Efficacy and Safety Superior to Placebo in Patients with Heart Failure (FINEARTS-HF) was designed to test the hypothesis that finerenone, in addition to usual therapy, would reduce the rate of total worsening heart failure events and death from cardiovascular causes among patients with heart failure and mildly reduced or preserved ejection fraction. Heart failure outcomes were improved, and hyperkalemia was not an issue. Epidermal growth factor mutations are common in non-small cell lung cancer. A deletion in exon-19 and the L858R mutation account for >80%. Amivantamab plus lazertinib (amivantamab-lazertinib) has shown clinically meaningful and durable antitumor activity in patients with previously untreated or osimertinib-pretreated EGFR (epidermal growth factor receptor)-mutated advanced non-small-cell lung cancer (NSCLC). In a phase 3, international, randomized trial, investigators assigned, in a

2:2:1 ratio, patients with previously untreated EGFR-mutated (exon 19 deletion or L858R), locally advanced or metastatic NSCLC to receive amivantamab-lazertinib (in an open-label fashion), osimertinib (in a blinded fashion), or lazertinib (in a blinded fashion). Amivantamab-Lazertinib improved progression-free survival in NSCLC patients with these mutations. Treatments for Dupuytren's contracture include limited fasciectomy and collagenase injection. Comparisons of the effectiveness of these treatments have been limited. Investigators performed an unblinded, multicenter, pragmatic, two-group, randomized, controlled noninferiority trial comparing collagenase injection with limited fasciectomy in persons with moderate Dupuytren's contracture. The limited-fasciectomy group did better than the collagenase-injection group. Chromodomain-helicase-DNA-binding protein 2 is an enzyme that in humans is encoded by the CHD2 gene. Mutations in CHD2 cause an epilepsy syndrome. CHASERR encodes a human long noncoding RNA (IncRNA) adjacent to CHD2, a coding gene in which de novo loss-of-function variants cause developmental and epileptic encephalopathy. Investigators report their findings in three unrelated children with a syndromic, early-onset neurodevelopmental disorder, each of whom had a de novo deletion in the CHASERR locus. The children had severe encephalopathy, shared facial dysmorphisms, cortical atrophy, and cerebral hypomyelination — a phenotype that is distinct from the phenotypes of patients with CHD2 haploinsufficiency. We learn a little bit more about the function of long noncoding RNAs. The N Engl J Med review is about "burn-out" in physicians. Physicians often enter medicine to help others but increasingly find that an excessive workload, administrative burdens, and the profit motives of insurance and pharmaceutical companies and health care systems are intractable barriers to improving patients' lives in the ways the physicians had envisioned. Amen to that! The N Engl J Med case is a 71-year-old woman was transferred to MGH hospital for neurosurgical evaluation because of confusion, aphasia, and a mass lesion in the brain. Not all masses are brain tumors. Tranexamic acid blocks the function of plasminogen and can help stem diffuse hemorrhage. Post-partum hemorrhage remains a problem, particularly in poor countries. We first inspect a randomized trial involving women with hemoglobin values <10 g/dL. Tranexamic acid did not improve outcomes in this study. Then, in a massive meta-analysis, we learn that tranexamic acid is helpful in reducing post-partum

hemorrhage after all. The Lancet then again addresses advanced cervical cancer. Cadonilimab is a new antibody that addresses both PD-1 and CTLA4. In a randomized trial, cadonilimab improved outcomes in patients with cervical cancer. Earlier, we had learned that nivolumab helps these patients as well. The Lancet case has neuroacanthocytosis. The Lancet review is about IL-23 driven autoimmune diseases. A second review is about climate change in cities. In Science Magazine we learn that antioxidant trials make some conditions, notably prostate cancer worse. Are all oxidants evil? Daily supplementation of drinking water with menadione sodium bisulfite-a water-soluble vitamin K3 precursor-effectively and durably reduced prostate tumor progression in mice. Then, the menadione oxidant also improved a rare, genetic muscle-disease model. Through a series of elegant in vitro studies, the authors demonstrated that menadione sodium bisulfite acts through a newly identified death process that is distinct from either mitochondrial or lysosomal cell death (apoptosis) pathways. Learn about the role of redox reactions and how this oxidant may help. Then, in the Washington Post, we are informed that "how long you can stand on one leg" effectively predicts falls in "older" people. Join me on Wednesday, October 23 for another stunning clinical journal club, 16:00 in English and 17:00 in German. Sincerely, Fred Luft

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